Quantification of left to right shunt in atrial septal defect using systolic time intervals derived from pulsed Doppler velocimetry

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SUMMARY Systolic time intervals derived from Doppler velocimetry measurements were used instead of direct pulmonary to systemic flow ratio measurements in adults with atrial septal defect to quantify left to right atrial shunts. Thirteen normal subjects and 25 patients with uncomplicated atrial septal defect confirmed by cardiac catheterisation were studied. The pulmonary to systemic flow ratio (Op:Os) expressing the shunt size was determined by the Fick method; in normal subjects the Op:Os ratio was assumed to be equal to 1.0. The pulsed Doppler analogue velocity recording of flow in the pulmonary artery and the ascending aorta was taken as indicating the ejection time of each ventricle and the O wave of the electrocardiogram as indicating the onset of systole. From these measurements the ratios of the pre-ejection periods to the ejection times (haemodynamic ratio) were calculated for each ventricle and the ratios of each variable (pre-ejection period, ejection time, and haemodynamic ratio) were calculated for both ventricles. Significant differences were found between the normal subjects and the patients with atrial septal defect for all these ratios. When the Doppler findings and the Fick measurements of Qp:Qs were compared the best linear correlation coefficient was for the left to right haemodynamic ratio. It is concluded that the use of a ratio involving several variables, such as the pre-ejection period and the ejection time for both ventricles, improves the reliability of this method, which appears to be applicable in adults.

All the Doppler techniques used so far for estimating blood volume flow in left to right shunts involve direct determination of both systemic and pulmonary blood flow. An excellent correlation is found between these measurements and those of invasive procedures in children.¹² Nevertheless, these measurements are less useful in adults, since the echocardiographic measurement of the arterial cross section is not routinely achieved.³

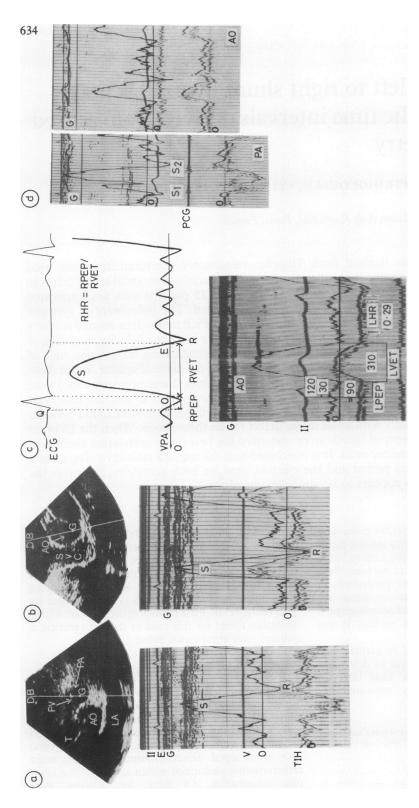
Systolic time intervals are related to cardiac output.⁴⁵ The purpose of this study was to determine whether the calculation of systolic time intervals derived from Doppler velocimetry measurements

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could lead to an alternative method of assessing atrial shunts in adults. Only a poor correlation (r=0.47) has been found between the ratio of both ejection times and the size of the shunt.⁶ In the present study we determined the correlation for all ratios, including those of the pre-ejection period to ejection time for both ventricles in order to involve the most significant anomalies found for this ratio in the left ventricle in patients with atrial septal defect.⁷

Patients and methods

The study population consisted of 13 normal subjects (seven women and six men, mean age 30 years) in whom any cardiac anomaly was ruled out by auscultation, radiography, and electrocardiography and 30 patients (16 women and 14 men, mean age 28 years) with atrial septal defect confirmed by right heart catheterisation performed within a week of the Doppler examination. Of these, five patients were



the systolic wave of the analogue trace to obtain the duration of the pre-ejection period (90 ms). (d) Calculation of the systolic time intervals from velocity recordings in the representation of the procedure used for calculation of the right systolic time intervals (for explanations, see text); lower panel: calculation of left systolic time intervals from a recording of the ascending aorta. The time delay of the analogue trace (30 ms) was subtracted from the interval between the Q wave of the electrocardiogram and the onset of how velocity displays. Both arterial recordings consist of a systolic wave (S) followed by a transient backflow wave (R). In the pulmonary artery (a) the systolic deflection is the pulmonary artery (a) in the transverse aorta short axis view and of the ascending aorta (b) in the suprasternal view. The Doppler beam is seen as a continuous white line Fig. 1 Recordings of the pulmonary and aortic flow velocity showing calculation of the systolic time intervals. (a) and (b) upper panel: cross sectional echocardiograms of (DB) and the Doppler gate as a white spot (G); lower panel: corresponding Doppler recordings with the M mode echocardiogram and the analogue (V) and spectral (TIH negative on the spectral display (blood flows away from the transducer) but was artificially reversed on the analogue display by a switch. (c) Upper panel: schematic pulmonary artery (PA) and the ascending aorta (AO) in a patient with atrial septal defect (case 2S) (mean values: 0·14 for the RHR, 0·48 for the LHR, with a LHR:RHR of 3.42 (invasive Op: Qs ratio 3.90).

analogue flow velocity trace of the pulmonary artery; RPEP, right pre-ejection period; RVET, right ventricular ejection time; RHR, right haemodynamic ratio; LPEP and T, tricuspid valve; PA, pulmonary artery; PV, pulmonary valve; LA, left atrium; AO, aortic orifice and ascending aorta; SVC, superior vena cava; II (ECG), lead II of LVET, left pre-ejection period and ejection time; LHR, left haemodynamic ratio; PCG, phonocardiogram; S₁ and S₂, farst and second heart sounds; distance between two the electrocardiogram; Q, Q wave of the ECG; E, M mode echocardiogram; V, analogue flow velocity recording; TIH, time interval histogram; O, zero line; VPA, vertical lines equals 40 ms (a, b, and d) and 10 ms (c). excluded from the study because of the presence of complete right bundle branch block, atrioventricular regurgitation, or associated pulmonary stenosis. The remaining 25 patients had uncomplicated ostium secundum. All the patients were in sinus rhythm and had incomplete right bundle branch block on the electrocardiogram; none had signs of cardiac failure.

HAEMODYNAMIC STUDY

Right heart catheterisation was performed in all patients and right and left cineangiography in nine. Pulmonary and systemic flow were determined by the Fick oxygen method. The size of the shunt was expressed as a ratio of the pulmonary to systemic flow (Qp:Qs). Dye dilution curves using an injection of indocyanine green (Cardiogreen) at the inferior vena cava-right atrial junction were also performed in order to exclude significant associated right to left shunts. The diagnosis was further confirmed at the time of operation in 10 patients. The size of the shunt ranged from 1.1 to 4.1. The right end diastolic ventricular pressure was normal in all cases. All patients except two had systolic pulmonary artery pressures ≤30 mm Hg, and all had normal values of pulmonary vascular resistance. Qp:Qs was assumed to be equal to 1.0 for normal subjects.

DOPPLER VELOCIMETRY

We used an ATL (Bellevue, Washington, USA) 3 MHz pulsed Doppler velocimeter combined with a cross sectional 90° wide angle mechanical scanner (ATL 851). According to the Doppler principle, the range gating system makes in possible to record the velocity of a small blood sample $(2 \times 4 \text{ mm})$ at any given location along the ultrasonic beam from 3 to 17 cm. The output we used in this study consisted of three signals⁸: (a) an audio signal of the Doppler shift, (b) the time interval histogram, and (c) the analogue flow velocity recording corresponding to the mean value of the Doppler frequency shift obtained by frequency to voltage conversion of the audio signal using the zero crossing detection technique; its polarity could be reversed by a switch on the recorder. The time delay introduced by the converter was approximately 30 (0.3) ms.9 We also used two video monitors, one for the real time scanning and the other for the Doppler display. Recordings were made on a Sony videotape recorder, with hard copies of real time imaging obtained on a 4633 Tektronics recorder. Doppler displays, M mode echograms, lead II of the electrocardiogram. and frequency selecting phonocardiograms were recorded on an IREX 101 (Mahwah, New Jersey, USA) multichannel recorder at paper speeds of 50, 75, and 100 mm/s. The potential error that these speeds could produce in the measurements was considered to be insignificant in relation

to the measured values.

The method used for combined cross sectional Doppler echocardiography involves (a) dynamic visualisation of the structures or chambers to be investigated, (b) positioning of the Doppler beam (seen as a continuous white line) in order to transsect the area of interest, and (c) adjustment of the Doppler gate (seen as a white spot) to control the depth of the sample volume along that beam. ¹⁰ The image is then frozen while the apparatus is automatically switched to the Doppler system. When the characteristic Doppler sound is heard, the recording may be performed.

Pulmonary flow velocity recordings (Fig. 1a)—We used the parasternal short axis view transsecting the heart at the level of the aortic valve orifice. Once the pulmonary orifice had been visualised we placed the gate into the pulmonary trunk, beyond the pulmonary valves, and carried out the recording.

Aortic flow velocity recordings (Fig. 1b)—We used the long axis suprasternal view of the ascending aorta,¹¹ visualising the aorta from the orifice to its connexion with the transverse aorta. In 11 patients only the upper part of the ascending aorta was visualised; the gate was then placed in this part of the vessel. In all cases the distance between the gate and the valve orifice did not exceed 3 cm.

MEASUREMENTS

Direct measurements of the systolic time intervals and calculation of the ratios were carried out.

Systolic time intervals (Fig. 1c)

Right pre-ejection period (RPEP)—The time interval (ms) between the Q wave of the electrocardiogram and the onset of the systolic wave of the pulmonary artery flow velocity trace was measured; 30 ms was subtracted from this interval in order to cancel the effect of the analogue delay.

Right ventricular ejection time (RVET) was measured from the onset to the end of the systolic wave of the pulmonary artery flow velocity recording.

Left pre-ejection period (LPEP) The time interval between the Q wave of the electrocardiogram and the onset of the systolic wave of the aortic analogue flow velocity trace was measured (minus 30 ms, as indicated for the pulmonary recording).

Left ventricular ejection time (LVET) was measured from the onset to the end of the systolic wave of the aortic analogue flow velocity recording.

For both aortic and pulmonary recordings, five consecutive cycles were measured to the nearest 5 ms by two independent observers and averaged to obtain the systolic time intervals for each subject. Care was taken to measure the right and left time intervals in relation to the same cardiac frequency and to the same phase of respiration (expiration) for each subject in order to avoid the effect of changes in cardiac rhythm

Table 1 Pulsed Doppler systolic time intervals and haemodynamic data in normal subjects and patients witn atrial septal defect

Case No	Age (yr)	Pulmonary artery pressure (mm Hg)			Qp:Qs ratio*	RHR	LHR	Ratios		
		s	D	М				LHR:RHR	RPEP:LPEP	RVET:LVET
					Norn	al subjects				
1	55				1.0	0.29	0-33	1-13	0-90	1.03
2	51				1.0	0.22	0.25	1·13 1·18	0.88	1.00
3	21				1.0	0-22	0-26	1-18	0-88	1.05
4	17				1.0	0-24	0-28	1.16	0.77	1.03
5	49				1.0	0.30	0.33	1-10	0.90	1.00
6	21				1.0	0.28	0-32	1.14	0.88	1.00
7	23				1.0	0.25	0-28	1-12	0-88	1.00
8	47				1.0	0.28	0-31	1.10	1.00	1.10
9	15				1.0	0.24	0-28	1.16	0-88	1.06
10	18				1.0	0-25	0.29	1-16	0-88	1.03
11	23				1.0	0-23	0-26	1.13	0-87	1.00
12	25				1.0	0-24	0.29	1.20	1.14	1.06
13	30				1.0	0-23	0.28	1·20 1·21	0-88	1.21
Mean	30					0-25	0.29	1-15	0-90	1.04
SD	14					0.03	0.03	0-03	0-09	0.06
					Patients with					
1	37	52	20	34	1.80	0.25	0.39	1.56	0.81	1.28
2 3	22	25	10	16	2.20	0.08	0-32	4.00	0-37	1.28
3	19	20	8	12	1.70	0.34	0-50	1.47	0-84	1.23
4	18	30	6	16	1.60	0∙25	0·50 0·28	2·00 2·33	0.61	1.23
5	52	85 20	40 8	55	2.10	0-12	0.28	2.33	0-44	1.00
6	49	20	8	12	1.50	0.25	0-40	1.60	0.75	1.20
7	25	32 28 28 25 15 20 30 23 30	13 8	21 6	1.50	0-19	0·32 0·33	1.68	0-77	1.28
8	14	28	8	6	2.45	0-14	0-33	2·35 2·17	0-55	1.29
9	18	28	12	18	3.00	0.23	0-50	2.17	0-69	1.46
10	21	25	12 8 10	15	1.60	0.26	0.50	1.92	0-66	1.25
11	27	15	10	12	3.00	0-13	0.41	3-15	0-50	1.50
12	17	20	13	14	4.10	0-12	0.45	3.75	0-36	1.33
12 13 14	42	30	20 12	22 14	3·50 2·20	0-13	0·39 0·39 0·63	3.00	0-45	1.28
14	18	23	12	14	2.20	0-16	0.39	2.43	0-61	1.38
15 16 17	22	30	14	16	1.80	0.36	0-63	2·43 1·75	0.78	1.36
16	25	26	13	17	2·60 2·75	0-13	0.35	2·69 2·56	0.50	1.28
17	26	19	6	11	2 ·75	0-23	0.59	2.56	0.53	1.36
18 19	20	19 22 30	10	14	1.60	0.20	0·35 0·59 0·31	1.55	0-77	1.17
19	46	30	13	18	2.10	0.25	0∙50	2.00	0-69	1.38
20	35	28	11	13	1.50	0.20	0.36	1.80	0-63	1-13
21	18	28 22	9	11	1.60	0.24	0.45	1.87	0-80	1-25
22	22	24 28 23	8	14	2.50	0.25	0.46	1.84	0-75	1.38
23	42	28	10	14	1.10	0-15	0-21	1.40	0-75	1.05
21 22 23 24 25	47	23	12	15	1.30	0-23	0-34	1.47	0.77	1-15
25	32	20	10	12	3.90	0.14	0-48	3-42	0-41	1.36
Mean	28	28	12	16	2.20	0-20	0-41	2.23	0-63	1.27
SD	11	13	6	9	0.81	0-07	0.10	0.74	0-15	0-12
p value						0.02	0.001	0.001	0-001	0-001

S, systolic; D, diastolic; M, mean; Qp:Qs, pulmonary to systemic blood flow; RHR, right haemodynamic ratio; LHR, left haemodynamic ratio; R(L)PEP, right (left) pre-ejection period; R(L)VET, right (left) ventricular ejection time.

*Assumed to be equal to 1.0 for normal subjects.

and in ventricular filling. The respiratory phase was noted by one observer.

Calculation of ratios

The following ratios were calculated from the previous measurements: (a) the right haemodynamic ratio (RHR) (RPEP:RVET) and the left haemodynamic ratio (LHR) (LPEP:LVET) and (b) the left haemodynamic to right haemodynamic ratio (LHR:RHR), the right pre-ejection to left pre-ejection period ratio (RPEP:LPEP), and the right

ventricular to left ventricular ejection time ratio (RVET:LVET).

STATISTICAL ANALYSIS

Statistical analysis was performed (Hewlett Packard 9815 A) using the mean values and standard deviation for each variable. The significance of the differences was assessed using Student's t test. Linear regression equations were also calculated to determine the correlation between the left and right ratios in the Doppler study and the Qp:Qs ratio from the haemodynamic

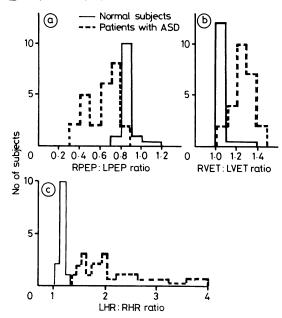


Fig. 2 Right and left ratios for systolic time intervals in normal subjects and patients with atrial septal defect (ASD): (a) RPEP:LPEP ratio: (b) RVET:LVET ratio; (c) LHR:RHR ratio. Distribution of subjects is shown per 0.2 unit of ratio.

measurements. The Doppler and haemodynamic study were performed independently by separate teams.

Results

There were no significant differences in age, sex ratio, and heart rate for both groups. No difficulties were encountered in recording both aortic and pulmonary flow velocities.

SYSTOLIC TIME INTERVALS (FIG. 2)

Table 1 gives the individual and mean values for normal subjects and patients with atrial septal defect; there were significant differences in the mean values of the latter group.

CORRELATIVE STUDY

The best linear correlation coefficient was found for the LHR:RHR ratio (y=0.87x + 0.25, standard error of the estimate 0.49, r=0.80, p<0.001) (Fig. 3a). Logarithmic transformation of the variables provided better distribution of the data. Figure 3b shows that the linear regression equation obtained using this transformation provided a better fit with the data (y=0.94x + 0.01, standard error of estimate 0.09, r=0.82). For the non-transformed data, we obtained the following 95% confidence interval for the mean

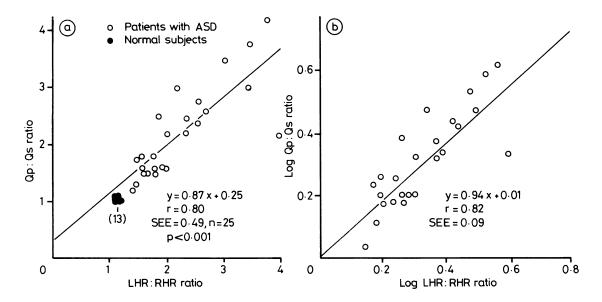


Fig. 3 Linear correlation between the size of the shunt expressed as the ratio of pulmonary to systemic flow (Qp:Qs) and the left to right haemodynamic ratio (LHR:RHR): (a) non-transformed data and (b) logarithmic transformed data for 25 patients with atrial septal defect.

Table 2 Linear regression equations between the pulmonary to systemic flow ratio and the right and left systolic time interval ratios in 25 patients with atrial septal defect

	Linear regression equations	Correlation coefficient (r)	SEE	p value
	Single ver	ntricle		
Right haemodynamic ratio (RHR)	v = -5.30x + 3.27	0.45	0.73	< 0.05
Left haemodynamic ratio (LHR)	$y = 2 \cdot 17x + 1 \cdot 30$	0-26	0.79	< 0.20
	Both ven	ricles		
LHR:RHR	y = 0.87x + 0.25	0-80	0-49	< 0.001
RPEP: LPEP	v = -3.89x + 4.66	0-72	0-57	< 0.001
RVET:LVET	y = 3.97x - 2.86	0-57	0-67	< 0.01

R(L)PEP, right (left) pre-ejection period; R(L)VET, right (left) ventricular ejection time.

value of y (Qp:Qs):1.58<1.73<1.90, when x (LHR:RHR) is equal to 1.77. For the single observation having a similar value of x, the 95% confidence interval for the value of y was: 1.14<1.73<2.60.

Table 2 gives the regression equations for the other ratios, and Table 3 the significance of the changes in these ratios according to the size of the shunt.

Discussion

In a previous Doppler study atrial septal defect was diagnosed using direct recordings of shunt flow velocity. ¹² In fact, direct quantification of the shunt from these recordings is not obtained, mainly because of inaccurate visualisation of the limits of the defect and the low energy of the flow signals. In children direct Doppler evaluation of the pulmonary to systemic flow ratio is better. In adults the pulmonary ¹³ or the aortic ¹⁴ flow below ¹⁵ or beyond the valves may be studied; but so far the routine application of this procedure to both vessels in such patients is hampered by frequent echocardiographic deficiencies. In contrast, velocity recordings either of valve motion or of arterial flow are quite easily performed in adults for both vessels. The Doppler technique thus offers an alternative

method of studying pulmonary and aortic outputs by determining systolic time intervals.

Systolic time intervals are influenced by several haemodynamic factors, of which cardiac output is a major one. This relation was first demonstrated by right and left heart catheterisation^{4 16} and then by non-invasive studies of both ventricles.¹⁷⁻¹⁹ Clearly, however, the timing of the events of the right heart in adults is much easier using the Doppler technique.^{20 21}

At present validation of the pulsed Doppler derived systolic time intervals by comparison with another non-invasive method has not yet been achieved for right heart values in adults because of the lack of a suitable non-invasive technique in this group of patients. Nevertheless, values for the right haemodynamic ratio in this study agree with those found by echocardiography and catheterisation in children; they were, furthermore, independent of age. ¹⁸ For left heart values a strong correlation (r=0.97) has been reported between phonocardiographic and Doppler derived systolic time intervals. ²² The Doppler technique is not affected by the transmission time interval since the sample is close to the valves and rules out the difficulties of identifying the

Table 3 Significance of the differences in mean (SD) values of ratios between normal subjects and patients with atrial septal defect according to the size of the shunt

Ratios	Normal subjects	(n=13)		Patients with atrial septal defect				
				<u>Op:Qs<2</u> (n=12)	<i>Op:Qs>2</i> (n=13)			
			Singl	e ventricle				
RHR	0.25 (0.03)		ŭ	0.24 (0.06)			0.16 (0.06)	
		t = 0.45	NS	` '	t = 3.48	< 0.01	, ,	
LHR	0.29 (0.03)			0.41 (0.11)			0.42 (0.09)	
		t = 3.73	< 0.01		t = 0.25	NS		
			Both	ventricles				
LHR:RHR	1.15 (0.03)			1.67 (0.20)			2.75 (0.67)	
	` ′	t = 9.55	< 0.001	` ,	t = 5.31	< 0.001	, ,	
RPEP: LPEP	0.90 (0.09)			0.75 (0.07)			0.53 (0.13)	
	, , ,	t = 4.95	< 0.001		t = 5.23	< 0.001		
RVET:LVET	1.04 (0.06)			1.22 (0.08)			1.33 (0.12)	
	(/	t = 6.05	< 0.001	(/	t = 2.76	< 0.02	(/	

R(L)HR, right (left) haemodynamic ratio; R(L)PEP, right (left) pre-ejection period; R(L)VET, right (left) ventricular ejection time; t, t values.

carotid incisura in cases of aortic regurgitation. The well known technological limitations of the pulsed Doppler technique⁸ are not relevant in this study since the technique was used only to determine the timing of cardiac events.

Our results in normal subjects regarding the ratios between both ejection times or both pre-ejection periods are consistent with those reported by Hirschfeld et al, 17 although in the latter study these ratios are expressed in reverse. Despite equal output from both ventricles the characteristics of right ventricular physiology are a shorter pre-ejection period and a longer ejection time than those of the left ventricle, 23 which explains the respective ratios. The calculation of the new ratio, the LHR:RHR ratio, highlights these physiological characteristics, which are less obvious in ratios between both pre-ejection periods or both ejection times.

Anomalies in left systolic time intervals have been found in patients with atrial septal defect. ^{7 24 25} Multifactorial statistical analysis showed that in such patients the most discriminant variables were the pre-ejection period and its ratio to the ejection time, the so called "left haemodynamic ratio." ²⁴ Changes in this ratio do not, however, reflect the size of the shunt. Decreased left ventricular filling due to the atrial shunt is likely to explain these findings.

Previous studies of right systolic time intervals have shown opposite values to those in the left ventricle—namely, a shorter pre-ejection period and a longer ejection time than is observed in normal subjects. 6 21 Both anomalies, although minor, lead to a significant decrease in the right haemodynamic ratio, which is more obvious in patients with large shunts (Tables 1 and 3).

Tsuda et al⁶ used the RVET:LVET ratio to estimate the size of the shunt with a correlation coefficient of 0.47 compared with 0.57 in this study. Two explanations may be suggested for this apparent discrepancy. Firstly, Tsuda et al's study involved only a few patients with small shunts, and the highest level of significance for the changes in the RVET:LVET ratio is found in precisely such cases (as shown in Table 3 for this ratio when Qp:Qs is <2.0). Secondly, Tsuda et al included several patients with pulmonary hypertension, which induces opposite changes in the right systolic time intervals.

Our study also shows that the best measurements for assessing the size of the shunt are the ratios between both ventricles and, in particular, the LHR:RHR ratio. This ratio involves two pairs of variables, the pre-ejection period and the ejection time; both of them are dependent on the changes in ventricular filling.⁴⁵ Thus the LHR:RHR ratio appears to combine the effect of the changes in both variables and in both ventricles. This is suggested by the higher

level of significance of the changes in this ratio than in those involving a single variable (Table 3). Our results suggest that most of the changes in the LHR:RHR ratio are induced by the increase in the RVET:LVET ratio in patients with small shunts and by the decrease in the RPEP:LPEP ratio in patients with large shunts. A typical illustration is case 5, a patient with pulmonary hypertension: the RVET:LVET ratio was 1.0 despite a shunt flow of 2.1, but this was offset by a pronounced decrease in the RPEP:LPEP ratio, and the LHR:RHR ratio was affected as expected.

In spite of a reasonably acceptable 95% confidence interval for the mean value of Qp:Qs, the 95% confidence interval that we obtained for the value of Qp:Qs for a single observation was wide. The reasons might have been due to the small size of the sample, the low rate of repeated values, and the increased variability of the data resulting from combining several variables, such as in the LHR:RHR ratio. This variable may, in rare cases, be a source of discrepancy, as it was in case 2, where an unaccountably decreased right pre-ejection period produced an erroneous result and in part contributed to this wide confidence interval. Further studies on larger groups of patients might yield narrower confidence intervals.

Clearly, the method we propose was not used in this study for diagnostic purposes but only for assessing the size of the shunt. In this context some factors might affect its reliability.

This method should be applied to uncomplicated atrial septal defect. Results should be interpreted with caution in patients with pulmonary hypertension, particularly when shunt flow decreases and pulmonary resistance is high. The results may also be affected in pulmonary stenosis, which causes an increased right ejection time²¹; the same limitation applies in the direct measurement of pulmonary flow in this condition.³ Some errors might be expected in atrioventricular regurgitation and heart failure since both conditions cause alterations in the systolic time intervals.⁵

The occurrence of incomplete right bundle branch block did not prolong the right pre-ejection period in our study. Whether complete right bundle branch block affects the results is unclear since its effect on the right pre-ejection period is not fully determined. Our selection criteria excluded such patients, although in two of them the right pre-ejection period was not increased.

Changes in systolic time intervals result from the effect of several simultaneous and sometimes conflicting factors. Our data suggest that relating several variables as a ratio is likely to highlight the effect of the predominant factor(s). In rare cases, however, the complex changes in the systolic time intervals may also produce discrepancies. This fact may partly

explain why the correlation coefficient in this study was lower than that obtained by direct measurement of flow in children.¹⁻³ The present method is, however, useful and applicable to adults.

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